REMARKS

Claims 1-16 are pending in the present Application. Claim 16 has been withdrawn. Claim 4 has been canceled, and Claims 1-3, and 5-15 have been amended, leaving Claims 1-3, and 5-15 for consideration upon entry of the present Amendment.

No new matter has been introduced by these amendments. Reconsideration and allowance of the claims are respectfully requested in view of the above amendments and the following remarks.

Examiner Interview

Applicant thanks the Examiner for the courtesy of an interview by telephone on May 8, 2007. Possible claim amendments to overcome the § 112, second paragraph, indefiniteness rejections were discussed.

Amendment to the Specification

The title has been amended as suggested by the Examiner to more clearly reflect the invention to which the claims are directed. The title has been amended to "GENOTYPING METHOD USING DNA CHIP" through the deletion of "robust" and "and DNA chip used therein". No new matter has been introduced by this amendment.

Amended Claims

Claims 1-3, and 5-15 have been amended to better define the invention. No new matter has been introduced by these amendments.

Claim 1 has been amended to include the limitations of Claim 4. Support for the amendment to Claim 1 can be found in claim 4 as originally filed, and in the specification (as originally filed) on page 4, line 17 bridging to page 5, line 14.

Support for the amendments to Claims 2 and 3 can be found on page 5, line 29 to page 6, line 3.

Support for the amendments to Claim 5 can be found on page 9, lines 17-21, and page 10, lines 9-12.

Support for the amendments to Claim 6 can be found in the claims as originally filed, and in the specification on page 6 line 20 to page 7, line 16.

Claim 7 was amended to better define the invention by removing the phrase "the genotyping algorithm using". Support for the amendment to Claim 7 can be found in the claims as originally filed.

Support for the amendments to Claim 8 can be found in the claims as originally filed and in the specification on page 7, line 10 to page 8, line 5; p. 8, lines 20-31, and page 9, line 27 to page 10, line 6.

Support for the amendments to Claim 9 can be found in the claims as originally filed and in the specification on page 7 lines 10-16, page 8, lines 9- 31, and page 9, line 27 to page 10, line 6.

Support for the amendments to Claim 10 can be found in the claims as originally filed and in the specification on page 6, lines 8-13.

Support for the amendments to Claim 11 can be found in the claims as originally filed and in the specification on page 6, line 20 to page 7, line 9, and p. 10, lines 20-23.

Support for the amendments to Claims 12 and 13 can be found in the claims as originally filed and in the specification on page 11, lines 1-17.

Support for the amendment to Claim 14 can be found in the claims as originally filed and in the specification on page 6, lines 8-13.

Claim 15 was amended to clarify the invention. Support for the amendment to Claim 15 can be found in the claims as originally filed.

Objections to the Claims

The Examiner has objected to Claims 5, 8, and 9 because of their grammatically awkward sentence structure and has requested appropriate correction. (Office Action dated 03/09/2007, page 2) In response to the Examiner's objections the following corrections have been made.

Claim 5 has been corrected to state "an input vector that is calculated" thereby replacing the objected to phrase "an input vector that are calculated".

Claims 8 and 9 have been corrected to state "components are independent of" thereby replacing the objected to phrase "components of the graph has a independence".

Claim Rejections Under 35 U.S.C. § 112, Second Paragraph

Claims 1-15 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. (Office Action dated 03/09/2007, page 4)

The Examiner has stated that Claims 1, 4, 5, 6, 7, 8, 9, and 11 recite the terms "using" or "used" which is vague and indefinite. (Office Action dated 03/09/2007, page 4) The terms "using" and "used" have been removed from claims 1, 5, 6, 7, 8, 9, and 11 in order to clarify the claims.

Regarding Claim 1, the Examiner has stated that "it is unclear if the probe pair is intended to be a probe pair comprising a wild type-perfect match probe and a mutant type-perfect match probe or a probe pair of a wild type-perfect match probe as well as an optimal probe pair of a mutant type-perfect match probe." (Office Action dated 03/09/2007, page 4) Claim 1 is now amended to define the invention more clearly. Specifically, the claim has been amended to clarify that "the optimal probe pair consists of a wild-type perfect match probe for a mutation site on the target nucleic acid and a mutant type-perfect match probe for the mutation site".

Regarding Claims 2 and 3, the Examiner has stated that the claims recite "each mutation site of the DNA chip" and "each mutation site of the DNA chip", respectively, and that these statements are vague and indefinite. (Office Action dated 03/09/2007, page 5) Claims 2 and 3 are now amended to more clearly define the invention and for consistency with claim 1.

Claim 4 has been deleted from the list of claims thereby rendering all rejections directed to this claim moot.

Regarding Claim 6, the Examiner has stated that the phrase "calculating the ratio between the hybridization intensity of the standard nucleic acid to the wild type-perfect match probe and the hybridization intensity of the standard nucleic acid to the mutant type-perfect match [sic]" is vague and indefinite. Office Action dated 03/09/2007, page 5) Claim 6 is now amended to define the invention more clearly.

Regarding Claims 6 and 8, the Examiner has stated that there is insufficient antecedent

basis for the limitation "the mutant type-perfect match". (Office Action dated 03/09/2007, page 6) Claims 6 and 8 claims are now amended to state "the mutant type-perfect match probe", thereby more clearly defining the invention.

Regarding Claim 8, the Examiner has stated that there is insufficient antecedent basis for "the products" and for "the vector". (Office Action dated 03/09/2007, page 6) The amendments to Claim 6 (from which Claim 8 depends) and to Claim 8 thereby now define the invention more clearly.

Regarding Claims 8 and 9, the Examiner has stated that there is insufficient antecedent basis for the limitation "the ratio components". (Office Action dated 03/09/2007, page 6) The amendments to Claims 6, 8 and 9 correct this antecedent basis issue and now define the invention more clearly.

Regarding Claim 11, the Examiner has stated that the phrase "calculating the ratio between the hybridization intensity of the target nucleic acid to the wild type-perfect match probe and the hybridization intensity of the target nucleic acid to the mutant type-perfect match [sic]" is vague and indefinite. (Office Action dated 03/09/2007, page 7) Claim 11 is now amended to define the invention more clearly.

Regarding Claims 12 and 13, the Examiner has stated that the limitations "the posterior probabilities" and "the greater posterior probability" are unclear as to what parameters are required and to what degree these parameters must be met to be considered greater. (Office Action dated 03/09/2007, page 7) Claims 12 and 13 are now amended to define the invention more clearly.

Regarding Claim 13, the Examiner has stated that there is insufficient antecedent basis for the limitation "the reliability requirement". Claim 13 is now amended to define the invention more clearly.

Regarding Claim 15, the Examiner has stated that the limitation "cross-hybridization data of the probe pair for each mutation site" is vague and indefinite. (Office Action dated 03/09/2007, page 8) Claim 15 is now amended to more clearly define the invention.

Applicants respectfully request a withdrawal of the rejections under 35 U.S.C. § 112, second paragraph, and an allowance of the claims.

<u>Claim Rejections Under 35 U.S.C. § 102(b)</u>

Claims 1-3, 5, and 15 stand rejected under 35 U.S.C. § 102(b), as allegedly anticipated by Mack (US 6,303,301 B1). Applicants respectfully traverse this rejection.

Amended Claim 1 is directed towards a genotyping method comprising an optimal probe pair selected by designing a plurality of probe pairs for the mutation site, wherein a probe pair consists of a wild type-perfect match probe and a mutant type-perfect match probe; immobilizing the plurality of probe pairs on a substrate to manufacture an optimal probe pair screening chip; hybridizing a standard nucleic acid to the optimal probe pair screening chip; collecting quantitative hybridization intensity data; calculating a value for each probe pair of the following equation: $\{Mean(\ln(r^{wt})) - 2\ SD(\ln(r^{wt}))/\sqrt{N^{wt}}\} - \{Mean(\ln(r^{mt})) + 2SD(\ln(r^{mt}))/\sqrt{N^{mt}}\}$ wherein N denotes a number of times hybridization of the standard nucleic acid has been performed; r^{wt} is a ratio between a hybridization intensity of a wild type standard nucleic acid to the wild type-perfect match probe and a hybridization intensity of the wild type standard nucleic acid to the mutant type-perfect match probe; r^{mt} is a ratio between a hybridization intensity of a mutant type standard nucleic acid to the wild type-perfect match probe and a hybridization intensity of the mutant type standard nucleic acid to the mutant type-perfect match probe; and *Mean* and *SD* denote a mean value and a standard deviation, respectively, of N ln(r) values, which are obtained by hybridizing the standard nucleic acid to the DNA chip N times; and selecting the probe pair having the largest value as the optimal probe pair.

To anticipate a claim, a reference must disclose each and every element of the claim. *Lewmar Marine v. Varient Inc.*, 3 U.S.P.Q.2d 1766 (Fed. Cir. 1987).

Mack teaches methods, compositions and apparatus for mapping the regulatory relationship among genes by massive parallel monitoring gene expression. (Abstract) Mack also teaches that the use of probe pairs composed of perfect and mismatched probes that serve as internal controls for hybridization specificity. (Col 34, lines 42-51) However, Mack does not teach each and every element of amended Claim 1. Specifically, Mack does not disclose a selecting an optimal probe pair as recited in amended Claim 1

Mack discloses the use of an algorithm that performs base identification of nucleotide changes between a sample and a reference, where the algorithm is based upon the effects that a single base change has on the array hybridization pattern of an experimental sample relative to a

wild-type reference. (Col. 39, lines 8-13) However, Mack does not disclose the details of the referenced algorithm. Further, Mack does not teach that selection of the optimal probe pair is based upon the probe pair that has the greatest value as determined by the equation in amended Claim 1. For at least these reasons, Mack does not teach each and every element of independent Claim 1 and dependent claims 2-3, 5, and 15 and thus, Mack cannot anticipate the claims.

Applicants respectfully request reconsideration and withdrawal of the §102(e) rejection over Mack and an allowance of the claims.

Double Patenting

Claims 1-15 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-14, and 17 of copending Application No. 11/019011.

Since neither the present claims nor the claims of the copending Application (No. 11/019011) have been patented, there is no way that double patenting can be determined (nothing is patented and there is no way to compare the final claims until one of the cases has been patented and the other claims are otherwise allowable). Hence, the Applicants respectfully request that the Examiner withdraw these provisional obviousness-type double patenting rejections until the claims are in final form and otherwise in condition for allowance, and the case over which double patenting is alleged is allowed. Until such time, there is no double patenting and no way to determine double patenting. MPEP § 804.01.I(B)(1).

It is believed that the foregoing amendments and remarks fully comply with the Office Action and that the claims herein should now be allowable to Applicants. Accordingly, reconsideration and allowance are requested.

If there are any additional charges with respect to this Amendment or otherwise, please charge them to Deposit Account No. 06-1130.

Respectfully submitted,

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